



Abdi, Alireza and Dalvand, Sahar and Vahedian-azimi, Amir and Ghanei Gheshlagh, Reza and Kurdi, Amanj (2018) Prevalence of depression among Iranian patients under hemodialysis; a systematic review and meta-analysis. Journal of Nephrology, 7 (4). pp. 224-232. ISSN 2251-8363 , 10.15171/jnp.2018.47.

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Journal of Nephropathology



Prevalence of depression among Iranian patients under hemodialysis: a systematic review and meta-analysis

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ARTICLE INFO

Article type:
Review

Article history:
Received: 10 January 2018
Accepted: 3 July 2018
Published online: 20 July 2018

Keywords:
Depression
Hemodialysis
Meta-analysis
Iran
End-stage renal disease
Renal failure

ABSTRACT

Context: Depression is a highly prevalent and debilitating mental disorder, particularly among patients under hemodialysis, who are more susceptible to depression due to their complex treatment regimens, dietary limitations, side effects of medications and fear of disease outcomes. This systematic review and meta-analysis explored the prevalence of depression in Iranian hemodialysis patients.

Evidence Acquisitions: In this systematic review and meta-analysis, search was done in national and international databases, including SID, MagIran, Google Scholar, Web of Science, Medline (via PubMed), and Scopus from inception to March 2018. Key search terms included hemodialysis, renal replacement therapy, dialysis, end-stage renal disease, renal failure, depression and Iran along with all their possible combinations. Data were combined for meta-analysis using random effects model. Heterogeneity between studies was analyzed by I² test, and data were analyzed by STATA (version 12) software.

Results: The included 24 articles had a sample size of 2941 participants; the overall prevalence of depression in hemodialysis patients in Iran was 56.8% (95% CI: 50.5-63). The results of the univariate meta-regression analysis showed no significant correlation between prevalence of depression and methodological quality of articles ($P=0.524$), duration of hemodialysis ($P=0.885$), publication year ($P=0.116$), mean age of participants ($P=0.224$) and sample size ($P=0.194$).

Conclusions: More than half of the hemodialysis patients in Iran suffer from depression. Given the overlap of depression symptoms with uremia in this group of patients, it is necessary to identify depression in these patients for early management and interventions.

Implication for health policy/practice/research/medical education:

Depression is common in patients undergoing hemodialysis, with an estimated prevalence of 56.8%. The presence of depressive symptoms could potentially decrease patient's medication adherence and hence leads to increased morbidity and mortality. Therefore, it is necessary for the healthcare team to always consider the symptoms of depression in hemodialysis patients to identify people at early stages and thus plan appropriate management care plan for better and effective outcomes.

Please cite this paper as: Abdi A, Dalvand S, Vahedian-Azimi A, Ghanei Gheshlagh R, Kurdi A. Prevalence of depression among Iranian patients under hemodialysis: a systematic review and meta-analysis. J Nephropathol. 2018;7(4):224-232. DOI: 10.15171/jnp.2018.47.

1. Context

Chronic kidney disease is a silent illness that is often undiagnosed until at advanced stages, when the only

treatment option is dialysis or kidney transplantation (1). Globally, the prevalence of end-stage renal disease (ESRD) is increasing, and it is doubled every 7 years (2).

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In Iran, 38000 patients are undergoing hemodialysis every year, and this number is estimated to be doubled by 2020 (3).

Management of ESRD requires strict lifestyle dietary changes and pharmacological regimens as well as commitments to regular attendance to hemodialysis sessions. Therefore, these patients face limitations in their social life, career, finances and independence (4). Furthermore, hemodialysis patients are susceptible to developing emotional problems due the chronic stress related to their disease burden, dietary and functional limitations, some of which are well-known risk factors for depression which include: (5) Fatigue, sleep disorder, treatment limitations, changes in family roles and social communications, limited daily activities, uncertainty about the future, unemployment, dependence on healthcare professionals and reduced sexual performance (6).

Due to high prevalence of mental disorders in hemodialysis patients, Levy used the term psychonephrology to introduce this disorder in patients with hemodialysis or renal failure (7). However, early diagnosis and assessment of depression is difficult in this patient group because depression and uremic symptoms overlap each other (5, 6). The interaction between chronic renal disease and depression is dynamic and multifactorial, given the common risk factors and biopsychosocial consequences of both illnesses, including similar biological changes in the immune system, inflammatory pathways, disruption of the hypothalamic-pituitary axis and sympathetic and parasympathetic changes (8).

Early diagnosis of depression in this patient group is essential since depression is reported to be associated with poor quality of life, increased re-hospitalization, cardiovascular diseases, malnutrition (6) and importantly, non-compliance with treatment (9) in hemodialysis patients. Mortality rate and non-compliance with treatment in hemodialysis patients suffering from depression are two to three times more than hemodialysis patients without depression (10). Previous studies in Iran reported conflicting results about the true prevalence of depression in hemodialysis patients, with prevalence ranging from 28% to 93% (11,12). Therefore, this study aimed to estimate the true prevalence of depression in hemodialysis patients in Iran using systematic search of literature. This is crucial because any strategy to prevent and manage depression in this group of patients requires accurate estimation of the size of the problem; hence appropriate allocation of healthcare resources.

2. Evidence Acquisitions

This study was a systematic review and meta-analysis,

of studies reporting the prevalence of depression in hemodialysis patients in Iran, published in Persian or English in national and international journals, from inception to March 2018. The SID, Magiran, Google Scholar, Web of Science, Medline (via PubMed), and Scopus data-banks were searched using the following key terms: hemodialysis, renal replacement therapy, dialysis, end-stage renal disease, renal failure, depression and Iran. Furthermore, the reference lists of the identified articles were also searched to identify any relevant studies.

2.1. Study selection and data extraction

All observational studies reporting the prevalence of depression in hemodialysis patients in Iran were included in the study. In cases where the prevalence of depression was compared between hemodialysis and kidney-transplant patients, the data of hemodialysis patients were extracted from the articles. The exclusion criteria comprised of articles not relevant to the subject, case reports, interventional studies, repeated studies and lack of access to the full-text articles.

To decrease bias, articles were screened independently by two researchers, and in the case of disagreement, another author who was an expert in meta-analysis reviewed the article. Then, the required data, including title, first author, publication year, study location, sample size, type of questionnaire, mean age, mean duration of dialysis and prevalence of depression were extracted from the articles. Articles were then screened and selected according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (13). The methodological quality of the articles was assessed using quality of life scale tool, which has been previously using in various studies. This tool consists of five items, including study design, comparison group, description of study samples, sample size and data collection. Each item is given a score of 0 to 3; with a higher score indicating a higher methodological quality (14-16).

2.2. Statistical analysis

Since prevalence has a binominal distribution, the variance of prevalence was calculated by the binomial distribution variance formula, and the mean weight was used to combine the prevalence rate of the various studies. To assess the heterogeneity of the selected studies, Cochran's Q and I² tests were applied (heterogeneities were classified into three categories, including <25% (low heterogeneity), 25-75% (moderate heterogeneity) and >75% (high heterogeneity). Considering the heterogeneity of studies and significant I² index, random effects model was used to combine the studies and

estimate the combined prevalence. Meta-regression analysis was performed to estimate the correlation of depression prevalence with the year of conducting the study and sample size, and analysis of subgroups was carried out to determine the prevalence rate of the five regions separately. Egger's test and Funnel plot were used to analyze publication bias. Sensitivity analysis was done by excluding a study one at a time. Data were analyzed by STATA software (version 12) and metan command.

3. Results

A total of 368 articles were identified from the initial search, 24 of which were included in the final analysis based on the inclusion and exclusion criteria (Figure 1). The studies selected for meta-analysis were examined in terms of sensitivity. The results showed exclusion of articles did not change the total estimate of prevalence of depression. To make sure all studies conducted on depression in hemodialysis patients in Iran were included in the study or not, the bias graph was used. The results of Egger's regression analysis showed no significant publication bias ($P=0.948$) (Figure 2).

A total of 24 articles with a total sample size of 2941 participants and a mean of 123 participants in each study were reviewed in this study. The maximum and minimum sample sizes were found for the studies by Nouruzi et al

($n=310$) (3) and Hashemi et al ($n=46$) (17), respectively. With regard to methodological quality, all the included studies were of moderate quality apart from two studies, one of which was poor and the other one was good. The general characteristics of the studies chosen for meta-analysis are shown in Table 1.

Overall, the prevalence of depression in hemodialysis patients was reported to be 56.8% (95% CI: 50.5-63) (Figure 3). The maximum and minimum prevalence rates of depression were found for a study carried out in Sanandaj (93%) (11), and one performed in Tehran (28%).

The findings of different depression screening tools showed the highest prevalence rates of depression in hemodialysis patients for the Center for Epidemiologic Studies Depression Scale (CES-D) and Depression Anxiety Stress Scale (DASS) (prevalence rate of 62%, 95% CI: 57-68) and Beck's Depression Inventory (BDI) (prevalence of 60%, 95% CI: 52-69). A total of 14 studies had used BDI. The results for the five regions of the country indicated the maximum and minimum prevalence rates of depression in hemodialysis patients for the region three (prevalence rate of 78%, 95% CI: 47-108) and region two (prevalence rate of 53%, 95% CI: 46-60), respectively (Figure 4). The prevalence of depression in the articles published in Persian language

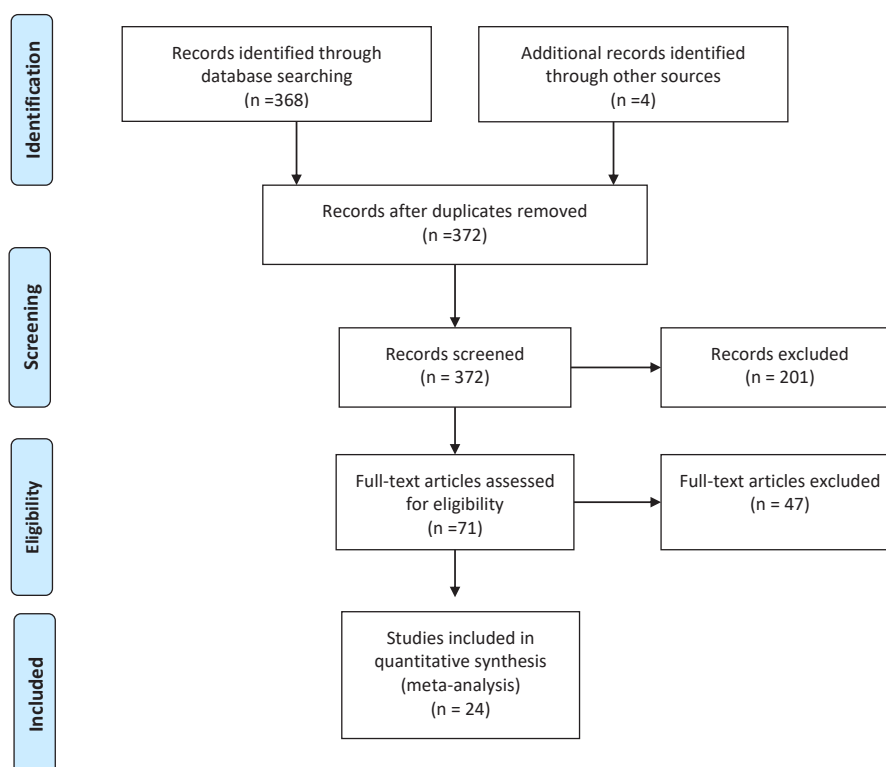


Figure 1. Screening and selecting the articles for meta-analysis based on PRISMA guidelines.

Table 1. Characteristics of the studies selected for meta-analysis

No.	First author	Year	Sample size	Mean age	Scale	Location	Prevalence of depression	Mean duration of hemodialysis (month)	Score of quality
1	Norozi Firoz (3)	2016	310	59.6±13.9	BDI	Mazandaran	44.8	39.8±42.5	9
2	Najafi (18)	2016	127	55.7±17.5	HADS	Tehran	31.5	-	8
3	Ekramzadeh (19)	2015	110	47.8±14.8	BDI	Shiraz	62	34.5±3.81	8
4	Anjomshoa (20)	2014	217	-	BDI	Kerman	57.4	-	7
5	Salehi (21)	2014	60	-	HADS	Mahabad	62	-	6
6	Hashemi (17)	2014	46	-	BDI	Shirvan	39.2	-	6
7	Osareh (9)	2014	150	56.4±16.4	BDI	Tehran	40.7	-	7
8	Bakhtiari (22)	2013	70	-	HADS	Tehran	64.3	-	4
9	Bayat (23)	2012	218	58.2±14.3	HADS	Isfahan	43.1	-	6
10	Sanavi (24)	2012	120	57.5±15.7	BDI	Tehran	70	5.42±3.36	6
11	Ahmadzadeh (25)	2012	196	-	SCL-90	Isfahan	50	-	5
12	Taraz (26)	2012	83	57.4±15.7	BDI	Tehran	61.4	71.1±57.3	11
13	Mogharab (27)	2011	60	54.4±17.5	BDI	Birjand	56.7	-	8
14	Roosbeh (28)	2011	196	-	SCL-90	Isfahan	50	-	6
15	Mahmoudi (11)	2010	61	47.4±15.5	BDI	Sanandaj	93	-	6
16	Afshar (29)	2010	120	57.6±15.3	BDI	Tehran	70	36.3±42.5	5
17	Mollahadi (30)	2010	147	39.3±11.7	DASS	Tehran	60.5	-	9
18	Masoudi Alavi (31)	2009	63	55.3±14.5	SCL-90	Kashan	65.3	30.3±36.8	8
19	Tavallaii (12)	2009	68	55.1±14.2	HADS	Tehran	27.9	-	8
20	Nazemian (32)	2008	150	30.1±2.91	CES-D	Mashhad	64.5	-	10
21	Raeisi (33)	2005	80	52.9±17.7	BDI	Tehran	60	55.9±56.6	4
22	Modanlou (34)	2005	129	-	BDI	Gorgan	68.2	-	7
23	Zahir aldin (35)	2005	100	-	BDI	Tehran	69	-	5
24	Salehi (36)	2003	60	-	BDI	Tehran	50	-	4

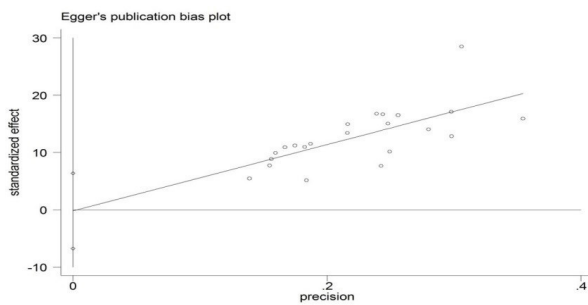


Figure 2. Publication bias in the studied articles. Circles show the weight of studies.

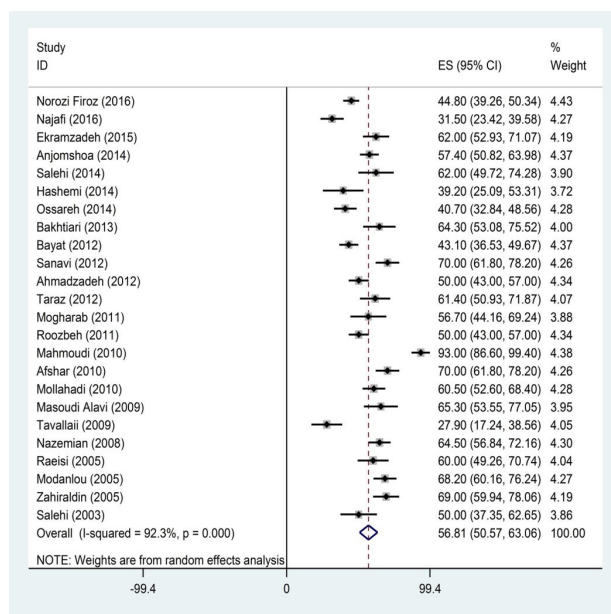


Figure 3. Forest plot of depression prevalence in hemodialysis patients. The confidence interval 95% for each study is shown as horizontal lines around the mean; dotted lines in the middle indicate total mean score and diamonds show the prevalence range of this disorder.

(prevalence rate of 63%, 95% CI: 56-71) was higher than that of articles published in English language (prevalence rate of 50%, 95% CI: 43-57). More details are illustrated in Table 2.

The results of the univariate meta-regression analysis showed no correlation between depression prevalence and methodological quality of articles ($P=0.524$), age of samples ($P=0.224$) and duration of hemodialysis ($P=0.885$). The prevalence of depression experienced a descending trend with an increase in the publication year ($P=0.116$) and sample size ($P=0.194$), but these changes were not statistically significant (Figure 5).

4. Discussion

In this meta-analysis, the prevalence of depression in

Iranian hemodialysis patients was 56.8% (95% CI: 50.5-63), which is higher than the prevalence rate reported for the U.S. (20%), Malaysia (36.6%) and China (29%) (37-39). Other studies have shown higher prevalence of depression in hemodialysis patients in neighborhood countries such as Iraq (80%), Pakistan (75%) and Saudi Arabia (63%) than in Iran (40-42). This variation could potentially be due to cultural, social and hygienic differences of the mentioned countries.

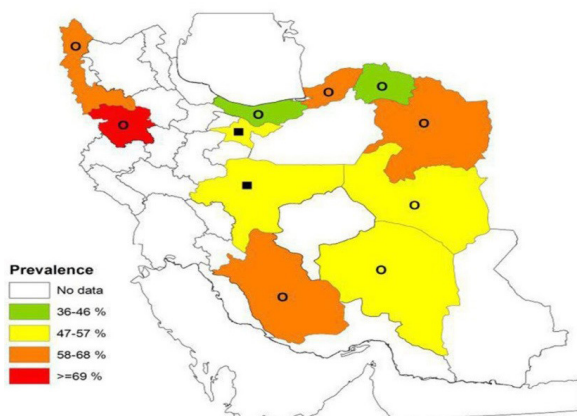
A study in 2015 showed a higher prevalence of depression in people with low education and socioeconomic status (43). Further, another study confirmed the association of depression with absence of appropriate physical activity (44). Since hemodialysis patients in Iran undergo critical conditions with regard to socioeconomic status, unemployment after the illness, stresses to access the required equipment and treatments (45) and lack of proper physical activity (46), high prevalence of depression is justifiable. Moreover, another issue that is quite important in hemodialysis patients is perceived social support in these patients. Patients with high social support experience less depression (47). Based on the studies carried out in Iran, considering the changing cultural and social conditions of the present age, less social support is provided to patients with chronic diseases (48), which is a potential risk factor for depression. Shahgholian et al reported that hemodialysis patients need spiritual, mental and physical support from the people around them and others' mere condolence was of no benefit to them. However, because of the social stigma of chronic disease for these patients and their families, their social communication is disrupted and families disregard and conceal the presence of hemodialysis patient to reduce the emotional load of this phenomenon and its effect on the future of the other members of the family, resulting in potential rejection of the patient by others and intensification of mental disorders in these patients (49).

In their meta-analysis, Mirzaei et al reported a prevalence rate of 63% (95% CI: 56-70) for depression in Iranian hemodialysis patients during 1998-2013, which indicates a descending trend for depression in hemodialysis patients in the recent years in comparison with the results of the present study. This meta-regression analysis also confirmed the correlation of depression with publication year (50). This declining trend in depression prevalence could be related to increased knowledge of people, increased health knowledge and more access to health facilities. The systematic review and meta-analysis of Palmer et al, also indicated a prevalence of 30% for depression among patients under hemodialysis,

Table 2. The prevalence of depression in hemodialysis patients

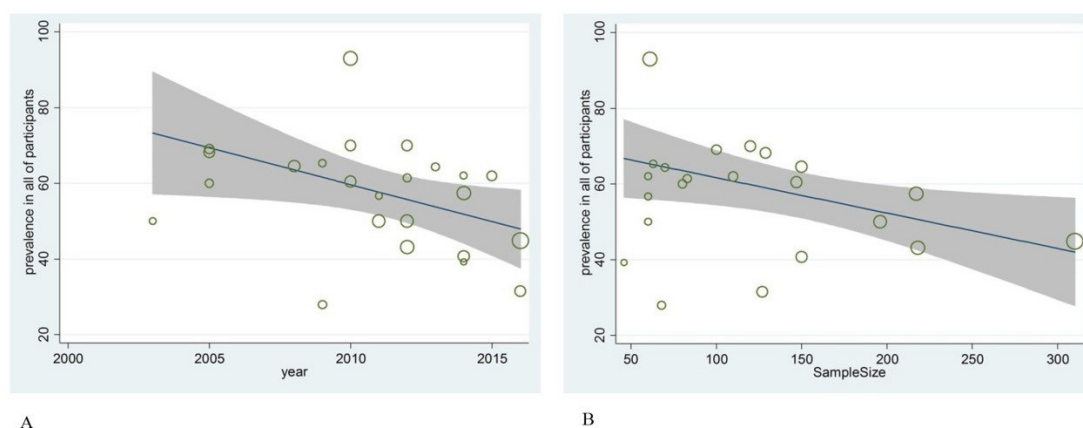
Groups	No. of Studies	Sample size	Prevalence (%)	95% CI	Heterogeneity		
					I ²	Q	P
Scale							
BDI	14	1646	60	52-69	92.9	183.29	0.0001
HADS	5	543	45	32-58	89.6	38.51	0.0001
SCL-90	3	455	54	46-62	63.8	5.53	0.063
DASS & CES	2	297	62	57-68	0	0.51	0.476
Language							
Persian	13	1271	63	56-71	89.6	115.73	0.0001
English	11	1669	50	43-57	89.4	94.55	0.0001
Region							
1	13	1564	55	47-63	91.1	135.43	0.0001
2	5	783	53	46-60	76.5	17.03	0.002
3	2	121	78	48-103	94.8	19.24	0.0001
5	4	56	56	47-64	68.9	9.66	0.022

Region 1: Alborz, Tehran, Qazvin, Mazandaran, Semnan, Golestan, and Gom; Region 2: Esfahan, Fars, Bushehr, Hormozgan, Kohgiluyeh and Boyer-Ahmad, and Chaharmahal and Bakhtiari; Region 3: West Azerbaijan, East Azerbaijan, Ardabil, Zanjan, Gilan, and Kurdistan; Region 5: Razavi Khorasan, North Khorasan, South Khorasan, Kerman, Yazd, and Sistan and Baluchestan

**Figure 4.** Prevalence of depression in hemodialysis patients for different provinces of Iran. Circles show provinces in which only one study has been done and squares indicate those with more than one study.

which is lower than the prevalence rate of depression in hemodialysis patients in Iran (51). Further, the systematic review and meta-analysis of Murtagh et al, showed a prevalence rate of 27% (95% CI: 5-58) for depression in hemodialysis patients (52).

High prevalence of depression in hemodialysis patients can be due to the overlap of physical symptoms of depression such as sleep disorder, anorexia, fatigue, sexual dysfunction and digestive disorders with uremia (41). On the other hand, depression is often undiagnosed in hemodialysis patients. Johnston believes that the symptoms of more than 70% of depressed hemodialysis patients are not diagnosed, or these patients are not referred to the healthcare centers for drug therapy or psychotherapy (53). One of the reasons for less attention of healthcare providers to depression in hemodialysis

**Figure 5.** Prevalence of depression in hemodialysis patients according to sample size (A) and the publication year of studies (B). Circles show the weight of studies.

patients is the low mood of these patients, which is due to the nature of their illness (42).

The findings of the five regions of the country showed the highest prevalence of depression (78%) for the hemodialysis patients of region three (two studies in Sanandaj and Mahabad). This difference could be attributed to the cultural characteristics of the people in this region, climatic conditions and access to healthcare services. The results of the study by Riolo et al indicated that prevalence of depression was not influenced by ethnicity and race (54). Some differences reported the previous studies are because of the different screening tools of depression being used. The results for separate tools showed the highest prevalence of depression for the articles that had used DASS, CES (62%) and BDI (60%). The lowest prevalence rate of depression was found in the studies that had used hospital anxiety and depression scale (HADS) (45%). Hospital anxiety and depression scale, with 14 items, analyses two dimensions, including depression and anxiety, and the final score is influenced by both depression status and anxiety status of the patient; whereas, BDI, with 21 items, focuses exclusively on affective, cognitive and physical aspects of depression. Comprehensive and updated presentation of depression prevalence in Iranian hemodialysis patients was one of the strengths of the current study. A limitation of this study was lack of access to the full text of several studies and low quality of some studies that had not reported the essential details of their research.

5. Conclusions

In general, the findings of this study showed that more than half of hemodialysis patients had the symptoms of depression. Considering the overlap of depression symptoms with uremia in these patients, diagnosis of depression in these patients is more difficult, and depression in these patients may be undiagnosed or may be diagnosed wrongly. The presence of depression as an underlying illness along with dietary limitations and tough treatment regimens could result in reduced quality of life and increased mortality in these patients. Knowledge of depression prevalence in hemodialysis patients can help the healthcare authorities to design programs and strategies to prevent, control and treat this disorder more effectively.

Acknowledgements

This study was taken from a research project approved by Kermanshah University of Medical Sciences (research ID; 3005990). The authors appreciate the research deputy of the concerned hospitals for their financial support.

Authors' contribution

AA and RGG participated in research design. AK and AV participated in the writing and editing of the paper. RGG and SD participated in performance of the research. SD participated in data analysis.

Conflicts of interest

The authors declare no conflict of interest. This study has not been published in or submitted to any other journal for publication.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

This study was funded by Kermanshah University of Medical Sciences.

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